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| 10/776,337 | 02/12/2004 | Changquan Sun | PC28117A | 1777 |
| 25533 7590 12/20/2007 PHARMACIA & UPJOHN 7000 Portage Road KZO-300-104 KALAMAZOO, MI 49001 | | | EXAMINER BARKER, MICHAEL P | |
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| | | | 12/20/2007 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/776,337

Applicant(s)

SUN ET AL.

Examiner

Michael P. Barker

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11/01/2007; Resp. to Restriction.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 19-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☒ Claim(s) 3, 4, 6-8, 10-12, and 16-18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 4/19/07.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application
- ☐ Other: _____.

DETAILED ACTION

Claims 1-28 are pending in this Application. **Claims 19-28** are withdrawn from consideration. This Office Action is based upon the merits of **Claims 1-18**.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 01/23/2007 was correctly filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the IDS was considered by the Examiner. Please refer to Applicant's copy of PTO-1449, submitted herewith.

Response to Remarks

Applicant's election with traverse of **Group II (Claims 2, 4-8, 13, 14, and 16** in the reply filed on 11/01/2007 is acknowledged. Applicant's traversal is found persuasive as it relates to the molecular entities embodied by polymorph I and polymorph II. Therefore, **Claims 1-18** will be examined together, and the merits of this Office Action is based upon these claims. The method claims, **Claims 19-28** remain withdrawn).

The traversal is on the ground(s) that Examiner has not shown the **Groups** to be distinct *and* independent from each other. This argument is not found persuasive. The issue of whether the Commissioner's instructions to examiners be revised to recite that inventions must be both "independent" and "distinct" to be properly restrictable was decided in *In re Lee, et al.*, 199 USPQ 108 (Comr's Dec. 5/26/78). The Commissioner held there need not be a showing that inventions are both independent and distinct to be properly restrictable. *Id.* at 109.

In the instant application, there is overlap between **Groups I and II** v. **Groups III and IV**; specifically, **Groups III and IV** require the use of the compounds/compositions claimed in **Groups I and II**. The inventions of **Groups I and II** are distinct since a reference anticipating the compounds/compositions of **Groups I and II** would not necessarily anticipate the methods of **Groups III and IV**. Therefore, **Groups I and II** are patentable over and thus distinct from **Groups III and IV**, such that if **Groups I and II** (drawn solely to compounds/compositions) issued as a separate patent than **Groups III and IV** (drawn to various methods of using the compounds/compositions), there would be no case for a double patenting rejection.

Thus, because of the reasons given in the restriction requirement, the requirement is still deemed proper and is therefore made FINAL.

Claim Rejections – 112, ¶2

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

- **Claims 1 and 2** are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: (1) The X-ray diffraction spectrum peaks, (2) a melting point, (3) IR spectroscopy data, (4) H-NMR spectroscopy data, and (5) DSC data.
- Likewise, **Claims 3 and 4** are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the

elements. See MPEP § 2172.01. The omitted elements are: (1) a melting point, (2) IR spectroscopy data, (3) H-NMR spectroscopy data, and (4) DSC data.

Please Note, amendments to include the aforementioned data in each of **Claims 1, 2, 3, and 4** would render **Claims 3 and 4** duplicative of **Claims 1 and 2**. Therefore, it is suggested that Applicant amend the independent claims by including the aforementioned data within the claim and cancel **Claims 3 and 4**.

- **Claims 5-12** are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: (1) The X-ray diffraction spectrum peaks, (2) a melting point, (3) IR spectroscopy data, (4) H-NMR spectroscopy data, and (5) DSC data.
- **Claims 5-12 and 18** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, **Claims 5-12** are each drawn to “A composition comprising polymorph [I or II] of a compound of formula I, wherein polymorph [I or II] comprises more than about [85 to 99] weight percent of the composition.”
 - The phraseology, "more than about" is ambiguous on its face.
- **Claims 13-17** are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See

MPEP § 2172.01. The omitted elements are: (1) The X-ray diffraction spectrum peaks, (2) a melting point, (3) IR spectroscopy data, (4) H-NMR spectroscopy data, and (5) DSC data.

Please Note: **Claims 13-17** are claimed as product-by-process claims. However, as polymorphs I and II are each singular entities, each with very distinct physical properties, the process portion of **Claims 13-17** is given no import. Even if Applicant makes amendments to include the aforementioned data, **Claims 13-17** would ultimately become duplicative of **Claims 1** and **2**. Therefore, it is suggested if Applicant's intention is to claim the process by which polymorphs I and II are made, amend **Claims 13-17**, such that these claims are process-claims, dependent upon **Claims 1** and **2**.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification (including knowledge readily known by a PHOSITA), while being enabling for solid compositions comprising polymorphs I or II, does not reasonably provide enablement for liquid compositions comprising polymorphs I or II. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In the formulation of a pharmaceutical composition, maintaining a polymorph is not automatic. Some polymorphs are more difficult to formulate than others because of their shape or hygroscopicity and the tablet can lose its bioavailability (see Rouhi, "The Right Stuff," Chem. & Eng. News (2003), p. 33, col. 2 – cited in Office Action filed 01/23/2007). Applicant's Specification fails to describe how the polymorph of **Claims 1 and 2** will be maintained in a pharmaceutical composition, namely a liquid pharmaceutical composition.

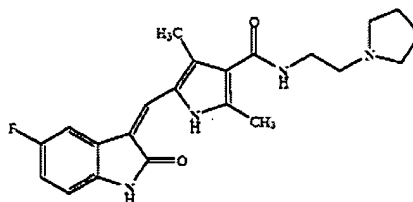
The term "composition" could be read to include liquid compositions. However, were "composition" read to include liquids, the structure of the polymorph would no longer exist. As this knowledge is widely known to a PHOSITA, it appears Applicant's "composition" claims are intended to include only solids. That said, it is suggested Applicant amend the composition claims to reflect the fact these compositions are indeed solid in form. While there is no guidance or support in Applicant's Specification supporting such an amendment to the claims, it seems such an amendment is not new matter, since it is well known in the art that polymorphs do not maintain their structural features in liquid form. Because polymorphs are known to break down in liquids, art rejections must be made over **Claims 5-12**.

Claim Rejections - 35 USC § 102(b)

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-12 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent

[0075] Compound Fifteen, below:



Publication No. 2002/0010203, which discloses

(p. 6, [0075]

and p. 21, XVII). The '203 publication discloses pharmaceutical compositions comprising the aforementioned compound (p. 13, [0149] – p. 15 [0183]).

Objections

Claims 3, 4, 6-8, 10-12, and 16-18 are objected to as they are based on a rejected base claim.

Conclusion

There is no prior art which anticipates or renders Applicant's claimed subject matter obvious. Prior to Applicant, polymorph I and II of a compound of formula I does not exist. The only substantive issues with the instant **Claims 1-18** are those of form, as well as inclusion of data specifically categorizing the two claimed polymorphs.

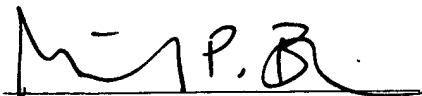
When **Claims 1-18** are in condition for allowance, Applicant may request rejoinder of the methods of **Claims 19-28**. However, at first blush, it would seem any method claims using any form of the compounds of formula I, including polymorphic forms, would be obvious in light of the fact this species of pyrrole substituted 2-indolinone is most likely known to exhibit protein kinase inhibition. Therefore, using a polymorphic form of a known compound for treating

disorders involved or associated with protein kinase inhibition would not produce an unexpected result.

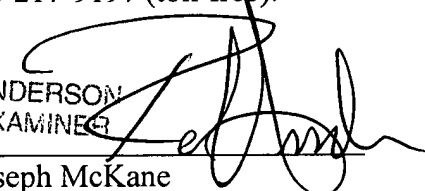
Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael P. Barker whose telephone number is (571) 272-4341. The examiner can normally be reached on Monday-Friday 8:00 AM- 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699. The unofficial fax phone for this group are (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is viable through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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